REMARKS

Status of the Claims

Claims 87-134, 137 and 140-157 are pending in the present application.

No new matter has been added. For instance, claim 132 has been amended to clarify the structure of the enzyme substrate and transferring enzyme as supported by the application as filed, especially page 28, first paragraph, original claim 49 and formulas C1-C4 at pages 28-29. Consistent changes have also been made to certain dependent claims. Moreover, claims 135, 136, 138 and 139 have been cancelled. Support may also be found at the same locations for newly added claims 148-157 as well as in original claims 51 and 52. Thus, no new matter has been added.

In view of the following remarks, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

Issues Under 35 U.S.C. § 102(b)/(e)

Claims 132-135 remain rejected under 35 U.S.C. § 102(b) as being anticipated by Bulter *et al.* (hereinafter referred to as Bülter).

Further, claims 132-139 remain rejected under 35 U.S.C. § 102(e) as being anticipated by DeFrees et al., U.S. Patent 7,265,084 (hereinafter referred to as DeFrees '084).

These rejections are respectfully traversed.

The present claims are directed to UDP-Gal/Glc structures, wherein Gal/Glc is 2-modified and either modified galactosyltransferase or GlcNAc/GalNAc-transferase is transferring the monosaccharide. In some of the newly added claims, the transfer is further specified as transfer to GlcNAc which is not disclosed in DeFrees '084.

Bülter fails to disclose 2-modified Gal(N) or Glc(N) comprising UDP-Gal(N) or UDP-Glc(N) structures. This is clear from the donor specificity of the enzymes disclosed in Bülter. With respect, Applicants point out that, in contrast to what is suggested by the Examiner, the teaching of Bülter is not useful with regard to preparation of 2-modified nucleotide-sugars. This is due to the fact that the specific enzyme galactose oxidase reacts only with the primary 6-position hydroxyl, not with secondary hydroxyls on positions 2, 3, or 4. Further, there is no analogous enzyme known for modification for secondary hydroxyls. Moreover, the Bülter pathway would lead to epimerization of the monosaccharide, if secondary hydroxyl would be

oxidized to a ketone. Thus, it is more than obvious that the methods of Bülter do not enable 2-modied nucleotide sugars.

Separately, Applicants submit that Bülter cannot prevent the patentability of the pending claims, at least in part due to the donor specificity of enzymes. Glycosyltransferases are in general known to have donor specificity capable of recognizing a single donor monosaccharide residue, and monosaccharides such as Gal or Glc differ only at one hydroxyl group position. It is obvious for a skilled person due to the donor specificity that Bülter cannot be generalized to any other positions. Moreover, the present invention does not claim regular galactosyltransferase, such as used in Bülter, but an engineered one. Bülter is testing a peptide GalNAc-transferase, but shows that it is actually inactive in transferring GalNAc. Indeed, Bülter tested several peptide GalNAc-transferases, but showed that these including polypeptide GalNAc-T3 were inactive in transferring 6-modified GalNAc (see page 890, 2nd column, 2nd paragraph of Bülter). Therefore, the teaching of both donor and enzyme of Bülter are inconsistent with, an indeed teach away, from the present invention.

DeFrees '084 includes a single example of UDP-GalN-hexanoyl-PEG and suggestion of transfer by GalNAc-T3, apparently to peptide on Scheme 14, page 204. There is no description of transfer to GlcNAc or carbohydrate. No known peptide transferring GalNAc transferase is β4-GalNAc-transferase. The present invention includes use of transferase capable transferring both GlcNAc and GalNAc not indicated in DeFrees '084. Furthermore, the engineered galactosyltransferase was not indicated by DeFrees '084, but teaching is directed to regular β4-galactosyltransferase. The inventors have tested bovine β4-galactosyltransferase for the reaction and it is not active similarily as in Bülter. Examples of DeFrees '084 refer to reactions with 6-modified Gal by bovine β4Galactosyltransferase. Therefore it is obvious that DeFrees '084 does not provide a working example and DeFrees '084 did not achieve functionality with regard to 6-modified or 2-modified monosaccharides.

Indeed, DeFrees '084 provides a suggestion of transferring monosaccharide derivative by bovine milk β1-4-galactosyltransferase (apparently only galactosyltransferase named in DeFrees '084, see paragraph [0832]). However, Bülter shows that this enzyme is an especially bad choice, even inactive with natural proteins which are indicated as substrates of DeFrees '084 (see Bülter page 888, column 1, 1st paragraph, lines 5-11, natural ovalbumin in Figure 7, page 889 v.s non-natural GlcNAc-albumin discussed in first paragraph, page 890) for the 6-modifed galactose

derivatives. DeFrees '084 does not show that this embodiment or any other hexose derivative would have functioned (see paragraph [1643] and [1565]). The practical examples of DeFrees '084 are towards inactive regular transferase variants for 6-modified galactose, with no example of 2-modified monosaccharides or engineered transferases or GlcNAc/GalNAc-transferase, especially for transfer to carbohydrate or GlcNAc, nor transfer in the presence of specific divalent cations, as shown by the present invention.

In view of the above, Applicants respectfully submit that the pending claims are patentable over the prior art cited by the Examiner.

Further, Applicants provide the following arguments concerning therapeutic compositions comprising enzyme and substrate:

Neither Bülter nor DeFrees '084 disclose a therapeutic composition. DeFrees '084 may use material in synthesis of pharmaceuticals but there is no indication that the reagents are aimed at modification of pharmaceuticals or for use as pharmaceuticals. Furthermore, specific divalent cation comprising therapeutic compositions are disclosed in the present invention and even more suitable Mg2+, Ca2+ or Zn2+ comprising compositions. The present invention further revealed therapeutic GlcNAc targets in tumors for cancer treatment and their accessibility for the transferase modification.

Applicants further point out that there is no evidence of reactions to cells or tissues in DeFrees '084. It is known that glycans on cell or tissue surfaces can be cryptic and not accessible for enzymes. Furthermore, an enzyme specific for the specific glycoconjugate available on the cell or tissue surface and additionally capable of transferring the modified monosaccharide would be needed (e.g. Bülter demonstrated substrate specificities of enzymes). Furthermore, alteration of the donor structure may affect the acceptors specificity. The present invention was first to demonstrate reactions with cells/tissues and 2-modifed monosaccharide residues.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Issue under 35 U.S.C. § 112, 1st Paragraph

Claims 132-141 stand rejected under 35 U.S.C. § 112, 1st paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed.

Applicants submit that the terms "enzyme substrate" and "transferring enzyme" are now limited to more clearly conform to the specific embodiments disclosed in the application as filed. As such, those of skill in the art would understand that Applicants were in possession of the claimed invention at the time of filing. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie, Registration No. 42874 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

By #42,874

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